

PENDING CLAIMS

Sub 1
1. Method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, with said method comprising:

- a) if need be, releasing, isolating or concentrating the polynucleic acids present in the sample;
- b) if need be amplifying the relevant part of the protease gene of HIV with at least one suitable primer pair;
- c) hybridizing the polynucleic acids of step a) or b) with at least one of the following probes:

probes specifically hybridizing to a target sequence comprising codon 30;

probes specifically hybridizing to a target sequence comprising codon 46 and/or 48;

probes specifically hybridizing to a target sequence comprising codon 50;

probes specifically hybridizing to a target sequence comprising codon 54;

probes specifically hybridizing to a target sequence comprising codon 82 and/or 84;

probes specifically hybridizing to a target sequence comprising codon 90;

or the complement of said probes,

further characterized in that said probes specifically hybridize to any of the target sequences presented in figure 1, or to the complement of said target sequences;

- d) inferring from the result of step c) whether or not a mutation giving rise to drug resistance is present in any of said target sequences.

2. Method according to claim 1, further characterized in that said polynucleic acids of step a) or b) hybridize with at least two of the said probes, or to the complement of said probes.

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3. (Amended) Method according to claim 2, further characterized in that said probes are chosen from the following list: SEQ ID NO: 7 to SEQ ID NO: 477, SEQ ID NO: 510 to SEQ ID NO: 519 or the complement of said probes.

4. (Amended) Method according to claim 1 further characterized in that said primer pair is chosen from the following primers: SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 and SEQ ID NO: 509.

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5. (Amended) Method according to claim 1 further characterized in that:

step b) comprises amplifying a fragment of the protease gene with at least one 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene, in combination with at least one suitable 3'-primer, and

step c) comprises hybridizing the polynucleic acids of step a) or b) with at least one of the probes specifically hybridizing to a target sequence or its complement, comprising codon 90.

6. (Amended) Method according to claim 1 further characterized in that:

step b) comprises amplifying a fragment of the protease gene with at least one 3'-primer specifically hybridizing to a target sequence located at nucleotide position 253 (codon 85) to position 300, in combination with at least one suitable 5'-primer, and

step c) comprises hybridizing the polynucleic acids of step a) or b) with at least one of the probes specifically hybridizing to a target sequence or its complement, comprising any of codons 30, 46, 48, 50, 52, 54, 82 and 84.

7. (Amended) Method according to claim 5, further characterized in that the 5'-primer is SEQ ID NO: 5 and the 3'- primer is one primer or a combination of primers chosen from the following primers: SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 and SEQ ID NO: 509.

8. (Amended) Method according to claim 6, further characterized in that the 5'-primer is one primer or a combination of primers chosen from the following primers: SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504 and the 3'-primer is SEQ ID NO: 6.

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9. (Amended) A probe as defined in claim 1 for use in a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample.

10. (Amended) A nucleic acid comprising a nucleotide sequence represented by any of the following SEQ ID numbers: SEQ ID NO: 478, SEQ ID NO: 479, SEQ ID NO: 480, SEQ ID NO: 481, SEQ ID NO: 482, SEQ ID NO: 483, SEQ ID NO: 484, SEQ ID NO: 485, SEQ ID NO: 486, SEQ ID NO: 487, SEQ ID NO: 488, SEQ ID NO: 489, SEQ ID NO: 490, SEQ ID NO: 491, SEQ ID NO: 492, SEQ ID NO: 493, SEQ ID NO: 494, SEQ ID NO: 495, SEQ ID NO: 496, SEQ ID NO: 497, SEQ ID NO: 498, SEQ ID NO: 499 and SEQ ID NO: 500; or a fragment thereof, wherein said fragment consists of at least two contiguous nucleotides and contains at least one polymorphic nucleotide.

11. (Amended) A primer for use in a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, comprising:

SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508, SEQ ID NO: 509; or

a 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene; or

a 3'-primer specifically hybridizing to a target sequence located at nucleotide position 253 (codon 85) to 300 of the protease gene.

12. (Amended) A diagnostic kit enabling a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, with said kit comprising:

a) when appropriate, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;

b) when appropriate, at least one of the primers comprising SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 or SEQ ID NO: 509; or

a 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene; or

a 3'-primer specifically hybridizing to a target sequence located at nucleotide position 253 (codon 85) to 300 of the protease gene;

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- c) at least one of the probes of claim 1 possibly fixed to a solid support;
 - d) a hybridization buffer, or components necessary for producing said buffer;
 - e) a wash solution, or components necessary for producing said solution;
 - f) when appropriate, a means for detecting the hybrids resulting from the preceding hybridization;
 - g) when appropriate, a means for attaching said probe to a solid support.
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3. (*Amended*) Method according to claim 2, further characterized in that said probes are chosen from the following list: [seq id no] SEQ ID NO: 7 to [seq id no] SEQ ID NO: 477, [seq id no] SEQ ID NO: 510 to [seq id no] SEQ ID NO: 519 or the complement of said probes.

4. (*Amended*) Method according to [any of claims 1 to 3,] claim 1 further characterized in that said primer pair is chosen from the following primers: [seq id no] SEQ ID NO: 3, [seq id no] SEQ ID NO: 503, [seq id no] SEQ ID NO: 504, [seq id no] SEQ ID NO: 4, [seq id no] SEQ ID NO: 506, [seq id no] SEQ ID NO: 507, [seq id no] SEQ ID NO: 508 and [seq id no] SEQ ID NO: 509.

5. (*Amended*) Method according to [any of claims 1 to 3,] claim 1 further characterized in that:

step b) comprises amplifying a fragment of the protease gene with at least one 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene, in combination with at least one suitable 3'-primer, and

step c) comprises hybridizing the polynucleic acids of step a) or b) with at least one of the probes specifically hybridizing to a target sequence or its complement, comprising codon 90.

6. (*Amended*) Method according to [any of claims 1 to 3,] claim 1 further characterized in that:

step b) comprises amplifying a fragment of the protease gene with at least one 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene, in combination with at least one suitable 5'-primer, and

step c) comprises hybridizing the polynucleic acids of step a) or b) with at least one of the probes specifically hybridizing to a target sequence or its complement, comprising any of codons 30, 46, 48, 50, 52, 54, 82 and 84.

7. (*Amended*) Method according to claim 5, further characterized in that the 5'-primer is [seq id] SEQ ID NO: 5 and the 3'- primer is one primer or a combination of primers chosen from the following primers: [seq id no] SEQ ID NO: 4, [seq id no] SEQ ID NO:

506, [seq id no] SEQ ID NO: 507, [seq id no] SEQ ID NO: 508 and [seq id no] SEQ ID NO: 509.

8. *(Amended)* Method according to claim 6, further characterized in that the 5'-primer is one primer or a combination of primers chosen [from] from the following primers: [seq id no] SEQ ID NO: 3, [seq id no] SEQ ID NO: 503, [seq id no] SEQ ID NO: 504 and the 3'-primer is [seq id no] SEQ ID NO: 6.

9. *(Amended)* A probe as defined in [any of claims 1 to 3,] claim 1 for use in a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample.

Please amend claim 10 by inserting a colon -- : -- following each "NO".

11. *(Amended)* A primer [as defined in any of claims 4 to 8,] for use in a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, comprising:

SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 503, SEQ ID NO: 504, , SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508, SEQ ID NO: 509; or

a 5'-primer specifically hybridizing to a target sequence located at nucleotide position 210 to 260 of the protease gene; or

a 3'-primer specifically hybridizing to a target sequence located at nucleotide position 253 (codon 85) to 300 of the protease gene.

12. *(Amended)* A diagnostic kit enabling a method for determining the susceptibility to antiviral drugs of HIV viruses in a biological sample, with said kit comprising:

- a) when appropriate, a means for releasing, isolating or concentrating the polynucleic acids present in said sample;
- b) when appropriate, at least one of the primers [of any of claims 4 to 6;] comprising SEQ ID NO: 3, SEQ ID NO: 503, SEQ ID NO: 504, SEQ ID NO: 4, SEQ ID NO: 506, SEQ ID NO: 507, SEQ ID NO: 508 or SEQ ID NO: 509; or